

receptor system. *Trends Neurosci.* **18**, 321-326 (1995).

5 9. Kaplan, D. R. & Miller, F. D. Signal transduction by the neurotrophin receptors. *Curr. Opin. Cell Biol.* **9**, 213-221 (1997).

10 10. Feinstein, E., Kimchi, A., Wallach, D., Boldin, M. & Varfolomeev, E. The death domain: a module shared by proteins with diverse cellular functions. *Trends Biochem. Sci.* **20**, 342-344 (1995).

15 11. Khursigara, G., Orlinick, J. R. & Chao, M. V. Association of the p75 neurotrophin receptor with TRAF6. *J Biol Chem.* **274**, 2597-2600 (1999).

20 12. Smith, R. A. & Baglioni, C. The active form of tumor necrosis factor is a trimer. *J. Biol. Chem.* **262**, 6951-6954 (1987).

25 13. Pietravalle, F., Lecoanet-Henchoz, S., Blasey, H., Aubry, J. P., Elson, G., Edgerton, M. D., Bonnefoy, J. Y. & Gauchat, J. F. Human native soluble CD40L is a biologically active trimer, processed inside microsomes. *J. Biol. Chem.* **271**, 5965-5967 (1996).

30 14. Tanaka, M., Suda, T., Takahashi, T. & Nagata, S. Expression of the functional soluble form of human fas ligand in activated lymphocytes. *EMBO J.* **14**, 1129-1135 (1995).

35 15. Liepinsh, E., Ilag, L. L., Otting, G. & Ibanez, C.F. NMR structure of the death domain of the p75 neurotrophin receptor. *EMBO J.* **16**, 4999-5005 (1997).

16. Gavrieli, Y., Sherman, Y. & Ben-Sasson, S. A.

Identification of programmed cell death in situ via specific labeling of nuclear DNA fragmentation. *J. Cell. Biol.* **119**, 493-501 (1992).

- 5 **17.** Baeuerle, P. A. & Henkel, T. Function and activation of NF-kappa B in the immune system. *Annu Rev Immunol* **12**, 142-179 (1994).
- 10 **18.** Carter, B. D., Kaltschmidt, C., Kaltschmidt, B., Offenhauser, N., Bohm-Matthaei, R., Baeuerle, P. A. & Barde, Y. A. Selective activation of NF-kappa B by nerve growth factor through the neurotrophin receptor p75. *Science* **272**, 542-545 (1996).
- 15 **19.** Taglialatela, G., Robinson, R. & Perez-Polo, J. R. Inhibition of nuclear factor kappa B (NFkappaB) actively induces nerve growth factor-resistant apoptosis in PC12 cells. *J. Neurosci Res.* **47**, 155-162 (1997).
- 20 **20.** Lezoualc'h, F., Sagara, Y., Holsboer, F. & Behl, C. High constitutive NF-kappa B actively mediates resistance to oxidative stress in neuronal cells. *J. Neurosci.* **18**, 3224-3232 (1998).
- 25 **21.** Stefanis, L., Troy, C. M., Qi, H., Shelanski, M. L. & Greene, L. A. Caspase-2 (Nedd-2) processing and death of trophic factor-deprived PC12 cells and sympathetic neurons occur independently of caspase-3 (CPP32)-like activity. *J Neurosci.* **18**, 9204-9215 (1998).
- 30 **22.** Fernandes-Alnemri, T., Litwack, G. & Alnemri, E. S. CPP32, a novel human apoptotic protein with homology to Caenorhabditis elegans cell death protein Ced-3 and mammalian interleukin-1 beta-converting
- 35

enzyme. *J. Biol. Chem.* **269**, 30761-30764 (1994).

- 5 **23.** Tewari, M., Quan, L. T., O'Rourke, K., Desnoyers, S., Zeng, Z., Beidler, D. R., Poirier, G. G., Salvesen, G. S. & Dixit, V. M. Yama/CPP32 beta, a mammalian homolog of CED-3, is a CrmA-inhibitable protease that cleaves the death substrate poly(ADP-ribose) polymerase. *Cell* **81**, 801-809 (1995).
- 10 **24.** Schlegel, J., Peters, I., Orrenius, S., Miller, D. K., Thornberry, N. A., Yamin, T. T. & Nicholson, D. W. CPP32/apopain is a key interleukin 1 beta converting enzyme-like protease involved in Fas-mediated apoptosis. *J. Biol. Chem.* **271**, 1841-1844 (1996).
- 15 **25.** Datta, R., Banach, D., Kojima, H., Talanian, R. V., Alnemri, E. S., Wong, W. W. & Kufe, D. W. Activation of the CPP32 protease in apoptosis induced by 1-beta-D-arabinofuranosylcytosine and other DNA-damaging agents. *Blood* **88**, 1936-1943 (1996).
- 20 **26.** Casaccia-Bonofil, P., Carter, B. D., Dobrowsky, R. T. & Chao, M. V. Death of oligodendrocytes mediated by the interaction of nerve growth factor with its receptor p75. *Nature* **383**, 716-719 (1996).
- 25 **27.** Bunone, G., Mariotti, A., Compagni, A., Morandi, E. & Della Valle, G. Induction of apoptosis by p75 neurotrophin receptor in human neuroblastoma cells. *Oncogene* **14**, 1463-1470 (1997).
- 30 **28.** Fields, S. & Song, O. A novel genetic system to detect protein-protein interactions. *Nature* **340**, 245-246 (1989).
- 35 **29.** Vojtek, A. B., Hollenberg, S. M. & Cooper, J. A. Mammalian Ras interacts directly with the

serine/threonine kinase Raf. *Cell* **74**, 205-214 (1993).

30. Ito, H., Fukuda, Y., Murata, K. & Kimura, A.
Transformation of intact yeast cells treated with
5 alkaline cations. *J. Bacteriol.* **153**, 163-168 (1983).

31. Gietz, D., Jean, A. S., Woods, R. A. & Schiestl,
R. H. Improved method for high efficiency
transformation of intact yeast cells. *Mol. Acids Res.*
10 **20**, 1425 (1992).

32. Schiestl, R. H. & Gist, R. D. High efficiency
transformation of intact cells using single stranded
nucleic acids as a carrier. *Curr. Gene.* **16**, 339-346
15 (1989).

33. Breeder, L. & Nasmyth, K. Regulation of the yeast
HO gene. *Cold Spring Harbor Sump. Quant. Biol.* **50**,
643-650 (1985).

20 34. Weiner, M. P., Felts, K. A., Simcox, T. G. &
Braman, J. C. A method for the site-directed mono- and
multi-mutagenesis of double-stranded DNA. *Gene* **126**,
35-41 (1993).

25